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APPLICATION NUMBER 08/247,746	FILED DATE 12/01/94	FIRST NAMED APPLICANT KAUSHANSKY	ATTY. DOCKET NO. 94-302
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12N2/0116

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EXAMINER
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MERTZ, P

ART UNIT	PAPER NUMBER
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1312

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DATE MAILED: 01/16/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

- ☒ Responsive to communication(s) filed on 10-25-96
- ☒ This action is FINAL.
- ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

- ☒ Claim(s) 1-13, 15-22, 24-30 is/are pending in the application.  
Of the above, claim(s) 1-8 is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 9-13, 16-24, 26-30 is/are rejected.
- ☒ Claim(s) 15, 25 is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

- ☒ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

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**Part III DETAILED ACTION**

1. Claims 14 and 23 have been cancelled in Paper No. 11 (10/25/96) and claims 1-8 are drawn to a non-elected invention. Claims 10-13, 16-17, 19-24, 26-27, and amended claims 9, 15, 18,  
5 25, 28-30 (Paper No. 11, 10/25/96), are pending and under consideration.

2. Receipt of applicant's arguments and amendments filed in Paper No. 11 (10/25/96) is acknowledged.

3. The following previous rejections and objections are withdrawn  
10 in light of applicants amendments filed in Paper No. 11 (10/25/96):  
(1) the rejection made under 35 U.S.C. § 103.

4. Applicant's arguments filed in Paper No. 11 (10/25/96) have been fully considered but persuasive in part. The issues remaining and new issues, are stated below.

15 5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

6. The disclosure is objected to because of the following informalities:

In claim 28, (second line), "adminstering", should be  
20 "administering", which appears to be a typographical error.

In claim 29, (second line), "adminstering", should be "administering", which appears to be a typographical error.

In claim 30, (second line), "adminstering", should be "administering", which appears to be a typographical error.

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Appropriate correction is requested.

7. Claims 9-13, 15-22 and 24-30 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth at pages 3-6 of the previous Office action (Paper No. 9, 4/19/96).

5           In subparts (b) and (c) of claims 9, 18, and 28-30, applicants claim "allelic variants" and "species homologs" respectively. With respect to claims 9, 18, and 28-30, the specification is not enabling for "allelic variants" since no reasonable expectation of success and no working example of non-naturally occurring variants  
10       of TPO have been provided in the specification such that fragments of the TPO polypeptide or substitution, deletion, or addition of a single amino acid residue would enable a protein of the biological characteristics of TPO. By application of the factors set forth in Ex parte Forman (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and  
15       reiterated in In re Wands (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) quantity of experimentation, (2) guidance presented, (3) the predictability of the art, and (4) the breadth of the claim, in the instant application, the quantity of experimentation to determine which other proteins are  
20       encompassed by the scope of the claims is practically infinite and the guidance provided in the specification very little, thereby rendering the results of the assays taught in the specification unpredictable. The claims are very broad, rendering the invention as claimed, unenabled by the specification. Therefore, it would

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require undue experimentation to determine which polypeptides having the biological activities of TPO would be encompassed by the scope of the claims in a method for stimulating erythropoiesis. The instant specification does not identify those of the 379 amino acid residues in the TPO polypeptide, which are essential for its biological activity and structural integrity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation of the 379 amino acid residues before they could even begin to rationally design a functional polypeptide having other than a natural amino acid sequence as disclosed in SEQ ID NO:4. The disclosure of a single natural amino acid sequence is clearly insufficient support under the first paragraph of 35 U.S.C. § 112 for claims which encompass a method for using every and all TPO polypeptides, including mutants thereof, since the novelty in the instant invention lies in the compound being used. In In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), the Courts have held that:

"Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since some improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that the scope of the claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the

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5 sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

Furthermore, the amount of embodiments corresponding to the TPO polypeptide recited in claims 9, 18, and 28-30, may be innumerable, and the enabled embodiment amounts to only one.

10 Therefore, there are substantial scientific reasons to doubt the scope of enablement, as set forth above. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. The specification does not describe a method of using any other TPO polypeptide other than the polypeptide having the  
15 amino acid sequence shown in SEQ ID NO:4, and since it is deemed to constitute undue experimentation to determine all the others, the disclosure is not commensurate with the scope of the claims.

20 With respect to the "species homologs" limitation in the claims, The present application does not demonstrate or provide an adequate written description for TPO polypeptides from any other mammalian species other than mouse and human. The issue here is that the specification does not provide the information sufficient to successfully enable the claimed method with other species of TPO other than mouse and human. To support this fact by the Examiner,  
25 evidence is being provided which discloses that human TPO is active on murine cells and vice versa but there appears to be no other information on other cross species activity (see pg. 247, lines 7-

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9, in The Cytokine FactsBook (1994), Robin Callard and Andy Gearing. Academic Press Inc. San Diego, CA). Therefore, since it is now known that there is only cross reactivity between murine and human TPO, it would not be possible for the skilled artisan to have knowledge of the cross reactivity between species homologs of TPO at the time the instant application was filed in a method for stimulating erythropoiesis comprising administering species homologs of TPO. It is unlikely that all species homologs of TPO would be enabled in the instant method because of the present knowledge that only human and mouse proteins have cross reactivity.

8. Claims 9, 18, 25, 28-30 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to provide proper antecedent basis for "proteins" in sub-part (a), when a TPO protein is being referred to in the preamble of the claims.

9. It is believed that all pertinent arguments have been addressed.

10. Claims 9-13, 16-17, 18-24, 26-30 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112 set forth in this Office action.

11. Claims 15 and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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12. Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. §706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

5 A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE  
10 EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED  
15 UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE  
ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE  
ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR  
RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL  
ACTION.

13. Any inquiry concerning this communication should be directed to Prema Mertz whose telephone number is (703) 308-4229. The examiner can normally be reached on Monday-Friday from 8:00AM to 4:30PM (Eastern time).

20 If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Stephen Walsh, can be reached on (703) 308-2957.

25 Papers related to this application may be submitted to Group 1800 in Crystal Mall 1 by facsimile transmission, in conformity with the notice published in the official Gazette, 1096 OG 30 (November 15, 1989). The FAX phone number for Art Unit 1812 is (703) 308-0294.

30 Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Prema Mertz Ph.D. P M  
Patent Examiner  
December 24, 1996



JOHN ULM  
PRIMARY EXAMINER  
GROUP 1800